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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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BIRCH STEWART KOLASCH & BIRCH
PO BOX 747
FALLS CHURCH, VA 22040-0747

EXAMINER

MURPHY, JOSEPH F

ART UNIT

PAPER NUMBER

1646

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14

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/492,361

Applicant(s)

JENTSCH, THOMAS J.

Examiner

Joseph F Murphy

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 1/8/2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-8,10-19,21-45,47 and 49-61 is/are pending in the application.
- 4a) Of the above claim(s) 12-17,31-45,47 and 49-58 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-11,18,19,21-30 and 59-61 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Formal Matters

1. Claims 9 and 20 were cancelled, and claims 1, 2, 5, 6, 8, 10, 11, 18, 19, 21, 22 were amended, and new claims 59-61 were added in Paper No. 13, 12/28/2001.

2. Claims 1-8, 10-19, 21-45, 47, 49-61 are pending. Claims 12-17, 31-45, 47, 49-58 stand withdrawn from consideration pursuant to 37 CFR 1.142(b). Claims 1-11, 18-19, 21-30, 59-61 are under consideration.

Response to Amendment

3. The rejection of claims 18-27 under 35 USC § 101 as being to non-statutory subject matter has been obviated by Applicant's amendment, and is thus withdrawn.

4. The rejection of claims 18-27 under 35 USC § 112 first paragraph as being non-enabled for in vivo transfection has been obviated by Applicant's amendment, and is thus withdrawn.

5. The rejection of pending claims 1-8, 10-11, 18-19, 21-30 under 35 USC § 112 second paragraph has been obviated by Applicant's amendment, and is thus withdrawn.

Claim Rejections - 35 USC § 112 first paragraph

6. Claims 2, 10, 11, 21, 22 stand rejected, and claims 1, 3-6, 10-11, 18-29, 59-61 are rejected, under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polynucleotide having a sequence as set forth in SEQ ID NO: 1, does not reasonably provide enablement for an isolated polynucleotide wherein the polynucleotide is at least 90% homologous to the nucleotide sequence set forth in SEQ ID NO: 1, for reasons of record set forth in Paper No. 12, 8/21/2001. Additionally, the specification provides insufficient

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enablement for an isolated polynucleotide capable of hybridizing under the conditions set forth in claim 1 to the polynucleotide sequence of SEQ ID NO: 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The rejection is based upon the evidence presented in the Mikayama et al. and Voet et al. references which demonstrates that the change of a single amino acid can radically alter protein function, and that because of this unpredictability of the protein art insufficient guidance is provided how to make or use the myriad of variant or mutated polypeptide species encoded by the claimed polynucleotides.

Applicant argues that i) an alignment of the disclosed sequence with known polypeptides enables the addition of mutations and ii) the 90% identical limitation enables and describes the claimed invention. However, in response to i) when given the broadest reasonable interpretation, the claims are clearly intended to encompass a variety of species including full-length cDNAs, genes and protein coding regions, because the claims encompass polynucleotides which hybridize to the claimed SEQ ID NO: 1. Clearly, it would be expected that a substantial number of the hybridizing or complementary polynucleotides encompassed by the claims would not share either structural or functional properties with a polypeptide encoded by SEQ ID NO: 1. The specification fails to provide an enabling disclosure for how one would use such polynucleotides. The specification provides insufficient guidance with regard to these issues and provides no working examples which would provide guidance to one skilled in the art on how to use the broadly claimed species. For the above reasons, undue experimentation would be required to make or use the claimed invention.

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In response to ii) Applicant argues that the 90% identical limitation enables and describes the claimed invention. However, it is clear that, although there is a 90% identity, there is a 10% dissimilarity between SEQ ID NO: 1 and the claimed polynucleotide sequences and the effects of these dissimilarities upon the structure and function of the encoded protein cannot be predicted. Bowie et al (Science, 1990, 247:1306-1310) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function and carry out the instructions of the genome and further teaches that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. (col 1, p. 1306). Bowie et al further teach that while it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (col 2, p. 1306).

Therefore based upon the Bowie et al. reference showing that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex, and the Mikayama et al. and Voet et al. references which demonstrates that the change of a single amino acid can radically alter protein function, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention.

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7. Claims 2, 10, 11, 21, 22 stand rejected, and claims 1, 3-6, 10-11, 18-29, 59-61 are rejected, under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for reasons of record set forth in Paper No. 12, 8/21/2001. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

The basis for the rejection is that these are genus claims, and that in the specification (page 5, lines 10), Applicants disclose that the mutated polynucleotide may be a polynucleotide of the invention having a nucleotide sequence encoding a potassium channel having an amino acid sequence that has been changed at one or more positions. The specification and claims do not indicate what distinguishing attributes shared by the members of the genus. Thus, the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted.

Applicant argues that i) an alignment of the disclosed sequence with known polypeptides describes the addition of mutations and ii) the 90% identical limitation enables and describes the claimed invention.

However, sequences identified by hybridization, as claimed in claim 1, would not predictably have the same structural and functional characteristics as the disclosed species

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because there is no way to determine what variations would be tolerated. Therefore, applicant has not disclosed sufficient species such that one skilled in the art would conclude that applicant was in possession of the claimed genus of polynucleotides which hybridize to, or are 90% identical to, SEQ ID NO: 1. Because the specification fails to describe a sufficient number of species of each genus, and because one of skill in the art could not be expected to predict the biological activity of the sequence variants encompassed by the claims, the written description requirement has not been met.

Claim Rejections - 35 USC § 102

8. Claims 1, 3-8, 10-11 and 18-19, 21-30 stand rejected, and new claims 59 and 61 are rejected, under 35 U.S.C. 102(b) as being anticipated by Singh et al. (1998), for reasons of record set forth in Paper No. 12, 8/21/2001.

The rejection of record is based on the teaching in Singh et al. which discloses the nucleotide and amino acid sequence of a potassium channel, KCNQ2, cloned from a fetal brain cDNA library (page 27, Figure 3). The nucleic acid taught in Singh et al. would hybridize under high stringency conditions to the nucleotide sequence SEQ ID NO: 1 of the instant application, thus anticipating claim 1. Applicant argues that the polypeptide encoded by the polynucleotide taught in Singh et al. is only 76% identical to the polypeptide disclosed in the instant Specification as KCNQ4. However, this limitation does not appear in claim 1, or any of the dependent claims. The polynucleotide of Singh et al. would hybridize under the conditions set forth in the claim, thus it meets all the structural limitations of the claim. The claim does not contain any functional limitations, thus the indicated claims are anticipated.

Claim Rejections - 35 USC § 103

Claims s 1, 3-8, 10-11 and 18-19, 21-30 stand rejected, and new claims 59 and 61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Singh et al. (1998) in view of WO 9401548 (Sibson et. al.), for reasons of record set forth in Paper No. 12, 8/21/2001.

Applicant argues that the polypeptide encoded by Singh et al. is only 76% identical to the polypeptide disclosed in the instant application as KCNQ4. However, as noted above, this limitation does not appear in the indicated claims, and the polynucleotide taught by Singh et al. meets the structural limitations set forth in the claims. Applicant further argues that Sibson et al. does not disclose any similarity to the sequences of the present invention. However, The test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference nor is it that the claimed invention must be expressly suggested in any one or all of the references; but rather the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

Conclusion

9. No claim is allowed.

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Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F. Murphy whose telephone number is 703-305-7245.

The examiner can normally be reached on M-F 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 703-308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
February 20, 2002


DAVID S. ROMEO
PRIMARY EXAMINER